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Birth room transition support for preterm infants: a Cochrane overview (Protocol)

Brown JVE, Walsh V, McGuire W

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[Overview of Reviews Protocol]

Birth room transition support for preterm infants: a Cochrane overview

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ABSTRACT

This is a protocol for a Cochrane Review (Overview). The objectives are as follows:

We will describe and summarise Cochrane Reviews of birth room interventions for preterm infants, and assess their methodological quality and the validity of their findings. We will map the evidence from Cochrane Reviews and identify important gaps in the evidence base. We will not compare multiple interventions with the intention of drawing inferences about their comparative effectiveness.

BACKGROUND

This Cochrane overview will focus on interventions to support postnatal transition in preterm infants, particularly very preterm infants (those born at less than 32 weeks' gestation) in whom the need for transition support is primarily due to surfactant insufficiency and respiratory distress syndrome. A separate Cochrane overview will focus on transition-support interventions for term and near-term infants (Brown 2019).

Description of the condition

One in ten newborn infants experiences delayed establishment of independent respiratory effort at birth that requires resuscitation or transition support. Reasons for ineffective or delayed transition to extra-uterine life, and need for support, differ with gestational age. In term and near-term infants, the main causes are respiratory distress due to incomplete clearance of lung fluid, and more serious perinatal complications including meconium aspiration, congenital infection, airway anomalies, or neonatal encephalopathy, which may be attributed to perinatal asphyxia (Vento 2010; Wyllie 2015; Wyllie 2016; Liley 2017).

Preterm infants, particularly very preterm infants (those born at less than 32 weeks' gestation), are more likely to experience "respiratory distress syndrome" of prematurity, as a consequence of lung surfactant deficiency and insufficient respiratory drive (Vento 2010; Sweet 2019). Compared with term infants, preterm infants lose more heat through environmental skin exposure due to having underdeveloped and thinner skin, with less body fat and brown fat for non-shivering thermogenesis, and less capacity for shivering and peripheral vasoconstriction. Hypothermia results in increased oxygen consumption and energy demand, increased acidosis from accumulation of lactic acid, and affects the circulation by altering peripheral resistance and cardiac output. (Knobel 2010).

Description of the interventions

In this review, we will consider a 'birth room intervention' to be any intervention that can be conducted immediately following the birth of the baby within the birth room (also called delivery room or delivery suite), without the requirement for prior transfer to the neonatal intensive care unit (or alternative setting) to be feasible to perform, or those that are not time critical and can be implemented after transfer to the postnatal setting (postnatal ward, nursery or neonatal unit). These interventions are typically categorised as airway, breathing, and circulatory support; administration of supplemental oxygen or other drugs; and measures to prevent hypothermia or metabolic compromise (Davis 2012; Perlman 2012) and are delivered by any of the healthcare professionals attending the birth (doctors, nurses, or midwives) as appropriate to the circumstances and complexity of the intervention.

- Airway management includes optimising head, jaw (and tongue) positioning to open the upper airway; removal of obstructing material such as mucus or blood from the oro- or naso-pharynx; and use of devices to ensure and maintain upper airway patency (oropharyngeal airway, laryngeal airway, endotracheal tube).
- Breathing support, when the airway is patent, includes positive pressure ventilation that can be delivered via various devices, with the aim of clearing the alveolar regions of lung liquid to allow gas exchange to occur (Hooper 2016).
- Circulatory support, though rarely required when airway management and breathing support has been successful, may include measures such as cardiac compression and intravascular volume replacement.
- Drugs - with the exception of supplemental oxygen administered during respiratory support, and exogenous surfactant replacement for infants with, or at risk of, respiratory distress syndrome - are rarely needed for resuscitation of preterm infants. They can include adrenaline (epinephrine) for infants with severe bradycardia or no detectable heartbeat, and dextrose to correct hypoglycaemia during prolonged resuscitation.
- Temperature conservation measures - which aim to prevent hypothermia-induced suppression of postnatal metabolic and physiological transition processes - include maintaining a high ambient temperature in the birth room, and use of thermal mattresses, radiant warmers, hats and blankets, with the additional use of occlusive wraps to minimise evaporative heat loss in very preterm infants.

How the intervention might work

Birth room interventions aim to optimise postnatal metabolic and physiological transition from the intra-uterine environment of low oxygen partial pressure to the extra-uterine environment of higher oxygen partial pressure, and to support respiration or ventilation to ensure pulmonary gas exchange and cardiac output sufficient for tissue oxygenation (Hooper 2016). Inadequate transition support may lead to worsening of hypoxia with consequent metabolic acidosis and compromised cerebral perfusion and oxygen delivery that increases the risk of mortality and neurological morbidity.

Birth room interventions work in several different ways and, while some apply to most infants in most situations (e.g. positioning for the head or jaw to establish airway patency), other interventions may be disease- or gestation-specific. Broadly, the level of support that may be needed is inversely related to the gestation of the newborn infant. Most moderate- to late-preterm infants, in the absence of additional complications such as meconium aspiration or infection, need only basic transition support measures such as airway positioning and stimulation. Very preterm infants may require more active support, including airway management and assistance with breathing. Extremely preterm infants (those born at less than 28 weeks' gestation), are more likely to require additional interventions, including positive pressure ventilation or surfactant replacement therapy (Fowlie 2004; Vento 2010; Sweet 2019).

Assessment and intervention to support postnatal transition can vary by context and setting (Davis 2012; Perlman 2012). Furthermore, the types of interventions available will differ according to health service resources, particularly in low-income countries where most preterm infants are born at home and typically without a skilled birth attendant. Low-income countries also have lower levels of antenatal surveillance and care, and a higher prevalence of maternal conditions that affect both maternal health and fetal growth and well-being (such as maternal infection); these factors influence the type of interventions most appropriate to those settings (Singhal 2012; Umphrey 2018).

Why it is important to do this overview

International consensus guidelines for newborn resuscitation and transition support are aligned with participatory training programmes to standardise context-appropriate practices (Wyllie 2015; Wyllie 2016; Liley 2017). Evidence exists, however, of marked variation in the use of transition-support practices between neonatal centres internationally (El-Naggar 2012; Mann 2012; Singh 2013). Consensus guidelines and recommendations for birth room transition support are increasingly informed by evidence from Cochrane Reviews (Wyllie 2015; Wyllie 2016; Liley 2017). The validity and utility of guidelines and policy recommendations is dependent on the quality of the included reviews. Variation exists in the methodological quality of Cochrane Reviews in several areas of health care, including perinatal and neonatal care (Al Faleh 2009; Willhelm 2013). As with any other type of study, methodological weaknesses (low internal validity) may introduce bias and limit the external validity and applicability of the findings. Guidelines or policy recommendations based on evidence derived from flawed reviews, especially given the perceived status of Cochrane Reviews as "high-level evidence", may drive or perpetuate poor practice and lead to adverse effects on outcomes for infants and families (Brok 2008; Meyer 2013).

Is an overview the correct approach?

Cochrane's Comparing Multiple Interventions Methods Group's "Editorial Decision Tree" suggests that an overview is an appropriate format to provide a "friendly front end" for users to access the synthesised evidence base (Methods Group's Editorial Decision Tree). The overview will describe multiple reviews of birth room interventions for newborn infants, appraise their validity and applicability, and identify gaps within the current suite of Cochrane Reviews.

OBJECTIVES

We will describe and summarise Cochrane Reviews of birth room interventions for preterm infants, and assess their methodological quality and the validity of their findings. We will map the evidence from Cochrane Reviews and identify important gaps in the evidence base. We will not compare multiple interventions with the intention of drawing inferences about their comparative effectiveness.

METHODS

Criteria for considering reviews for inclusion

We will include systematic reviews published in the *Cochrane Database of Systematic Reviews*, which assess birth room transition-support interventions (i.e. interventions delivered to the newborn in the same location as the birth took place) for newborn infants born before 37 weeks' gestation, including, but not limited to: airway support, ventilatory (breathing) support, circulatory support, drug interventions, and thermoregulatory interventions. Standard care, existing intervention, placebo, no treatment, an alternative intervention or any other comparator will be eligible.

Reviews will be eligible for inclusion regardless of number, type, and methodological quality of studies included. Eligibility will not be restricted by outcomes reported. We will report the primary and secondary outcomes as defined in individual reviews; we anticipate that these will include mortality and major morbidity, including long-term neurodisability and impairment.

We will not include reviews of interventions that are more usually or feasibly delivered following admission of the preterm infant to the neonatal unit (if needed), or reviews of birth room interventions administered as part of routine practice to all infants.

Search methods for identification of reviews

We will search the lists of reviews published by Cochrane Neonatal and Cochrane Pregnancy & Childbirth, as available on their respective websites (Cochrane Neonatal; Cochrane Pregnancy and Childbirth). No other databases will be searched. The search will be conducted independently by two overview authors (VW and JVEB). Any disagreements will be resolved through discussion and arbitration with a third author (WM). We will consult the editorial teams of Cochrane Neonatal and Cochrane Pregnancy & Childbirth to ensure all relevant reviews are included. The study identification and selection process will be illustrated in a flowchart.

Data collection and analysis

We will use the standard methods of Cochrane for data collection and synthesis, according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Selection of reviews

Two overview authors (VW and JVEB) will assess the included systematic reviews independently. We will resolve any disagreement through discussion with a third author (WM) until consensus is reached.

"Out of date" reviews

Reviews will be assessed for eligibility regardless of publication date or date of the last search. For reviews older than five years (those published in 2013 or earlier), we will contact the corresponding author by email only to check if an update is planned or in progress, and inform them of our intention to include their review in our overview. We will make reasonable efforts to establish the current status of all reviews published before 2013. If two emails to the corresponding author (sent two weeks apart) do not receive a reply, we will contact the responsible editorial team to ascertain if the review in question is due to be updated or if an update is already in progress. We will document and publish the results of our enquiries. We will include a category of "status unclear" for any reviews older than five years for which we do not know the update status. If an update is planned or underway, we will include the review in a "being updated/update planned" category, and state a date when the update is expected whenever possible. If an update is not planned (as confirmed by the authors or the editorial team, or both), we will distinguish between the following categories.

- Reviews that are no longer being updated because the topic area is deemed to be fully understood or new evidence is highly unlikely to emerge: we will follow the authors' and editorial teams' assessment of this without running our own literature search for possible new evidence. For the purposes of our overview, these reviews will be deemed up-to-date (despite being older than five years old) and will be included in our synthesis.
- Reviews that the authors and editorial teams acknowledge should be updated but for which there are no current plans for updating: we will include these reviews in our overview in an "update needed" category and will include any updates in a

future update of the overview. We will highlight these reviews to the responsible editorial team and urge them to prioritise these titles for updating.

Overlapping or competing reviews

We do not expect to find overlapping or competing reviews (i.e. reviews that address the same question or include some or all of the same primary studies), as we are limiting our searches to Cochrane Reviews. Should we find two or more eligible reviews that address the same clinical question, we will only include the most recent one in our overview.

Protocols

Registered Cochrane protocols and titles will be identified and classified as "ongoing reviews". We will contact the appropriate Cochrane editorial team to establish expected completion dates of any relevant reviews with published protocols.

Data extraction and management

We will extract the following data from each included Cochrane Review.

- Title, author, publication date, date of most recent search/ update.
- Population (gestational age and birth weight, setting).
- Intervention(s) and comparator(s).
- Outcomes reported.
- Number of studies included.
- Number of participants included.
- Quality of the included studies (as assessed by the review authors).
- Results of the review, focusing on the following outcomes: death prior to hospital discharge, morbidity (necrotising enterocolitis, bronchopulmonary dysplasia, retinopathy of prematurity, infection), and neurodevelopmental outcomes at any time after discharge (most likely reported at 18 to 24 months and at school starting age).
- Discrepancies between review protocol and publication (Page 2014).
- Methodological quality, risk of bias and any other limitations of the review.
- GRADE assessments of certainty of evidence for review primary outcomes.

Data extraction will be carried out by one overview author and checked by another. Disagreements will be discussed or assessed by a third party until consensus is reached. Data will be extracted electronically into a piloted form and "Characteristics of included reviews" and "Overview of reviews" tables will be produced. We will contact the authors of eligible reviews to request any missing data, but will not attempt to make contact with authors of any of the primary studies included in eligible reviews.

Dual authorship

We may include Cochrane Reviews that were authored by members of the overview team. This is a potential source of bias (Büchter 2016). We will identify any Cochrane Reviews that share one or more authors with this overview and ensure that the eligibility of such reviews is checked by a member of the of the overview team who is not affiliated with the review(s) in question. We will ensure similar safeguarding procedures are in place for quality assessment. The potential impact of including Cochrane Reviews affected by dual authorship will be addressed in the discussion of the overview.

Assessment of methodological quality of included reviews

We will use the AMSTAR 2 tool (Shea 2017; Appendix 1) to assess the methodological quality of the included reviews. To further assess the risk of bias of the systematic reviews, we will use the ROBIS tool (Whiting 2015; Appendix 2). Quality assessment will be carried out by one overview author and checked by another. Disagreements will be discussed until consensus is reached. In line with guidance provided by the developers of the AMSTAR 2 tool, we will not produce an overall quality score but will instead assess methodological quality as high/moderate/low/critically low (Shea 2017).

We will check included reviews against their protocols to enable assessment of methodological transparency and rigour. Particular attention will be paid to outcomes prespecified in the review protocol versus outcomes reported in the published review. Any discrepancies between protocols and published reviews that were not reported as amendments to the protocol in the publication will be reported.

We will not reassess the quality of included primary studies within reviews but instead will report study quality according to the review authors' assessment. We will collect this information during the data extraction process, including the quality assessment tool used and the authors' overall conclusions.

Data synthesis

We will provide a narrative description of the characteristics of the included Cochrane Reviews, organised (where possible) as interventions for neonates born: 1) preterm; 2) very preterm or very low birth weight; and 3) other specific groups of 'at risk' neonates. Where possible, we will aim to describe interventions used in specific settings (high-income countries versus low- or middle-income countries).

We will summarise the main results of the included reviews by categorising their findings using the framework adopted in a Cochrane

overview of interventions to prevent cerebral palsy (Shepherd 2018), as follows.

- Effective interventions: the review found high-quality evidence of effectiveness for an intervention.
- Promising interventions (more evidence needed): the review found moderate-quality evidence of effectiveness for an intervention, but more evidence is needed.
- Ineffective interventions: the review found high-quality evidence of lack of effectiveness for an intervention.
- Probably ineffective interventions (more evidence needed): the review found moderate-quality evidence suggesting lack of effectiveness for an intervention, but more evidence is needed.
- No conclusions possible: the review found low- or very low-quality evidence, or insufficient evidence to comment on the effectiveness of an intervention.

We do not envisage undertaking indirect or mixed treatment comparisons within the overview but will assess if there is a need for a network meta-analysis to be undertaken at a later date.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. AMSTAR 2

1. Did the research question and inclusion criteria for the review include the components of population, intervention, control group, and outcome (PICO)?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search strategy?
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions?
8. Did the review authors describe the included studies in adequate detail?

9. Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review?
10. Did the review authors report on the sources of funding for the studies included in the review?
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?
12. If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or other evidence synthesis?
13. Did the review authors account for risk of bias in individual studies when interpreting/discussing the results of the review?
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
15. If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for the review?

Appendix 2. ROBIS

Phase 1: assessing relevance
Phase 2: identifying concerns with the review process
DOMAIN 1: study eligibility criteria
1. Did the review adhere to predefined objectives and eligibility criteria?
2. Were the eligibility criteria appropriate for the review question?
3. Were eligibility criteria unambiguous?
4. Were any restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?
5. Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?

DOMAIN 2: identification and selection of studies
1. Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?
2. Were methods additional to database searching used to identify relevant reports?
3. Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?
4. Were restrictions based on date, publication format, or language appropriate?
5. Were efforts made to minimise error in selection of studies?

DOMAIN 3: data collection and study appraisal
1. Were efforts made to minimise error in data collection?
2. Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?
3. Were all relevant study results collected for use in the synthesis?
4. Was risk of bias (or methodological quality) formally assessed using appropriate criteria?
5. Were efforts made to minimise error in risk of bias assessment?

DOMAIN 4: synthesis and findings
1. Did the synthesis include all studies that it should?
2. Were all predefined analyses reported or departures explained?
3. Was the synthesis appropriate given the nature and similarity in the research questions, study design and outcomes across included studies?
4. Was between-study variation (heterogeneity) minimal or addressed in the synthesis?
5. Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?
6. Were biases in primary studies minimal or addressed in the synthesis?

Phase 3: judging risk of bias
RISK OF BIAS IN THE REVIEW
1. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4?
2. Was the relevance of identified studies to the review's research question appropriately considered?
3. Did the reviewers avoid emphasising results on the basis of their statistical significance?

CONTRIBUTIONS OF AUTHORS

All authors contributed to the development of the protocol.

DECLARATIONS OF INTEREST

JVEB: none known.

VW: none known.

WM: none known.

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Internal sources

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External sources

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